

REMARKS/ARGUMENTS

Reconsideration of this application is requested. Claims 15, 23, 24 and 30 – 45 will be pending in the application subsequent to entry of this amendment. The allowability of claims 17, 18 and 20-22 (now, effectively claims 33, 34 and 36 – 38) is noted with appreciation. Applicants submit that all of the pending claims are allowable for the reasons explained in more detail below.

Amendments to the Claims // New Claims

The claims have been amended in order to more particularly point out and distinctly claim that which applicants regard as their invention; new claims have been added to preferred aspects of the disclosure; claims have been amended to respond to the Examiner's rejection on page 3 of the Action.

In claim 15 minor amendments have been made for style and typographical reasons.

Claims 16 and 25-29 have been deleted.

New claims 30-32 have been added. Claim 30 is substantially the result of incorporation of former claims 24 and 28. Claim 31 is substantially former claim 28. Claim 32 is substantially former claim 29.

New claims 33-44 have been added.

Claim 33 comes from the limitation of previous claim 15 by incorporation of previous claim 17.

Claim 34 corresponds to previous claim 18.

Claim 35 corresponds to previous claim 19.

Claim 36 corresponds to previous claim 20.

Claim 37 corresponds to previous claim 21.

Claim 38 corresponds to previous claim 22.

Claim 39 corresponds to previous claim 23.

Claim 40 corresponds to previous claim 24.

Claim 41 corresponds to new claim 30, but referred to new claim 33.

Claim 42 corresponds to new claim 31, but referred to new claim 33.

Claim 43 corresponds to new claim 32, but referred to new claim 33.

Claim 44 is substantially the result of incorporation of former claims 24 and 29.

Claim 45 is substantially former claim 29.

No new matter has been added.

Claims 15-45 are pending.

Enablement 35 USC §112

Claims 25-29 have been deleted.

New claims 30-32 and 41-44 have been added. Support for these claims is found in the specification; *see* in particular page 4, second paragraph, page 6 second and last paragraphs, pages 13 and 14, mostly important the passage on pages 14-16, *Effects on Saccharomyces cerevisiae...*, and pages 16-17.

The subject-matter of claim 45 was determined to be enabled by the Examiner; *see* Office Action, page 3, first two lines.

Arguments presented in the previous replies of October 24 and 29, 2008 are herein repeated with some modifications.

It is well known to the skilled person that camptothecins act as anticancer agents by inhibiting of Topoisomerase I. In this sense, a reference was made in the present application to European Patent No. EP1044977 as a review of camptothecins and their use as anticancer agents. A copy of this patent is on record; *see* the IDS filed on January 13, 2006.

Also of record are the following papers:

Clin canc res, 2002; *PNAS*, 1993, 1839; *Exp Opin Ther Pat*, 2002, 837; *Cancer Res.*, 1999, 2939, *Mol Pharm*, 2000, 243; *J med Chem*, 2001, 3264; *Blood* 1993, 1146; *Blood*, 1993, 571; *Cancer Control*, 2000, 548;

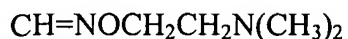
showing that the claimed compounds act on cancer through the inhibition of Topoisomerase I.

Thus, the person with ordinary skill in the field of pharmacology will find exhaustive information, taken from the present description and the above prior art, to make the invention, in particular for treating a cancer sensitive to topoisomerase inhibitor, by administering the compounds of claim 15 or claim 33. In view of the above applicants believe that all the method of treatment claims overcome the rejections under 35 USC § 112.

Novelty 35 USC §102(b)

The interpretation of the Dallavalle et al. reference by the Examiner is not accurate.

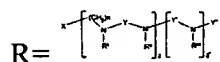
Compound # 22 in the reference bears in position 7 the substituent:



Which, when read on the formula I in claim 15 provides:

$$m = 0$$

$\text{CH}=\text{N}-\text{R}$, wherein



$$z = 0$$

$$z' = 1$$

$$\text{Y}' = (\text{CH}_2)_{n1}$$

$\text{Y}'' = \text{no definition available: CH}_3 \text{ is not present in claim 15}$

$$\text{X} = \text{O}$$

$$n1 = 2$$

$\text{R}^{\text{III}} = \text{no definition available: CH}_3 \text{ is not present in claim 15}$

The only definition available for CH_3 (alkyl) is for:

R^{VI} , which is part of the group COR^{VI} , $\text{NHCO}_2\text{R}^{\text{VI}}$;

R^{VIII} and R^{IX} , which are part of the group $\text{NR}^{\text{VII}}\text{R}^{\text{IX}}$, which is an optional substituent of

Ar.

Therefore, compound 22 of Dallavalle et al. cannot read on claim 15.

The same arguments are applied to the Penco et al. reference.

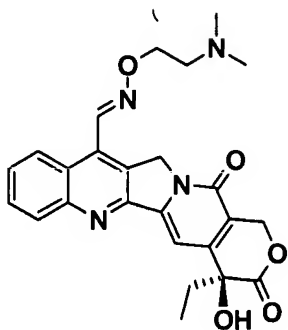
The protective groups of the present claims are never alkyl.

The protective groups of the present claims are:

$\text{CO}_2\text{R}^{\text{VI}}$; $\text{CO}_2\text{CH}_2\text{Ar}$; CO_2 -(9-fluorenylmethyl); $(\text{CH}_2)_{n5}\text{-NHCO}_2\text{R}^{\text{VI}}$; CH_2Ar ; COAr ;
 $(\text{CH}_2)_{n5}\text{-NHCO}_2\text{CH}_2\text{Ar}$; $(\text{CH}_2)_{n5}\text{-NHCO}_2$ -(9-fluorenylmethyl).

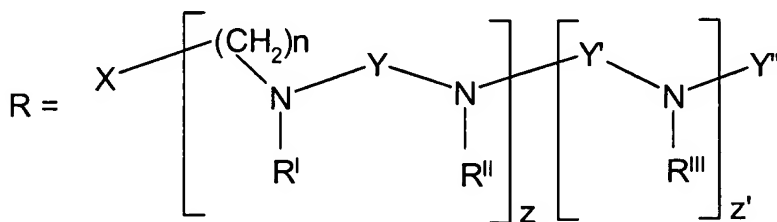
Applicants wish to further clarify the issue of novelty by comparing the chemical formula of the prior art compound 22 of Dallavalle S., *et al.*, *J. Med. Chem.*, **2001**, 44, 3264.

Indeed, compound 22 (depicted in the figure below) does not fall within the herein claimed invention under examination.



Compound 22

It is clear that the 7-(*N,N*-dimethylaminoethoxy)iminomethylcamptothecin (compound 22), is not included within Formula I, whatever the meanings of the various radicals of the R moieties of formula I compounds are, as explained below:



As a skilled person will understand, to get "compound 22", the following conditions **have** to be verified:

X = O, Z = 0, Z' = 1, Y' is (CH₂)_n, n₁ = 2 together with R^{III} and Y'' being both methyl. However, the latter condition cannot be met because of the impossibility of these two radicals to adopt such a meaning, as explained above.

Accordingly, also claims 19, 23 and 24 are novel over the cited reference.

Withdrawal of this rejection is respectfully requested.

Applicants are pleased to note that the subject matter of previously presented claims 17, 18 and 20-22 was indicated as allowable by the Examiner

New claim 33 is the result of incorporation of the limitations of claim 17 into claim 15.

Claims 34-38 correspond to allowable subject-matter indicated by the Examiner.

Claims 39 and 40 are referred to an allowable claim.

Double patenting

GIANNINI ET AL.
Appl. No. 10/564,637
May 5, 2009


For the reasons presented above, there is no overlap between the cited references and the present claims. Therefore, the rejection is moot.

Allowance of the application is respectfully requested. Should the examiner require further information, please contact the undersigned.

Respectfully submitted,

NIXON & VANDERHYE P.C.

By: _____


Arthur R. Crawford
Reg. No. 25,327

ARC:eaw
901 North Glebe Road, 11th Floor
Arlington, VA 22203-1808
Telephone: (703) 816-4000
Facsimile: (703) 816-4100